

Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claim 1 has been amended, claims 3-5 have been cancelled without prejudice, and new claims 10-21 have been added. Descriptive support for new claims 10 and 11 appears in the first full paragraph on page 30 and the third full paragraph on page 35, respectively; descriptive support for new claims 12-14 appears in the first full paragraph on page 34; and descriptive support for new claims 15 and 16 appears in the first full paragraph on page 30. New claim 17 finds descriptive support in original claim 3 (i.e., claim written in independent form), and new claims 18-21 find descriptive support in original claims 4 and 6-8, respectively. Claims 1, 2, and 6-21 are pending.

The objection to the specification is overcome by the above amendments. Although applicants disagree with the assertion made by the U.S. Patent and Trademark (“PTO”), the present claim language is clearly supported by the first full paragraph on page 30, along with the disclosure of the nucleic acid sequence of SEQ ID NO: 181 and the corresponding amino acid sequence of SEQ ID NO: 182.

The objections to claims 1 and 5 are overcome by the above amendments and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) (“[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.”). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO’s conclusion

cannot be based on genus size alone. But that is precisely what the PTO has done at pages 3-4 of the outstanding office action. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

In contrast, applicants present Exhibits 1-3 (attached hereto) as evidence that the nucleic acid sequence of SEQ ID NO: 181 and the corresponding amino acid sequence of SEQ ID NO: 182 represent the claimed genus. Exhibit 1 is a presentation of a Genbank accession for a thermophilic *Bacillus*, or *Geobacillus*, *dnaX* nucleic acid that is homologous to the nucleotide sequence of SEQ ID NO: 181. This *dnaX* nucleic acid was identified by a protein-protein BLAST search of the Genbank database performed using the amino acid sequence of SEQ ID NO: 182 and the BLAST default settings. Homologous sequences were identified in a number of *Bacillus* species, including from the thermophilic *Geobacillus kaustophilus* (Exhibit 1). Based upon alignments performed using Align[®] for nucleic acids and ClustalW for amino acids (using the European Molecular Biology Laboratory server and its default settings), this homolog shares about 99 percent identity at the nucleic acid level (Exhibit 2) and about 99 percent identity at the amino acid level (Exhibit 3). Thus, species of tau subunits from thermophilic organisms that belong to the biological classification *Bacillus* or *Geobacillus* clearly share similar structure and, therefore, function.

Applicants submit that the language recited in claims 1 and 9 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, but merely described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only the one rat species disclosed), and the larger genus of 'vertebrate' cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Bacillus* or *Bacillus stearothermophilus*) and the specification describes one or more species within that genus. Claims 1 and 9 recite the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claims 1 and 9 (and claims dependent thereon) find written descriptive support in the present application.

It should be noted that the “Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, ‘Written Description’ Requirement,” make explicitly clear that the description of a representative number of species does *not* require the description to be of such a nature that it would provide support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Hence, the absence of sequences (in the present specification) for the later-identified *dnaX* and tau homologs is irrelevant to the issue of whether the present specification provides adequate written descriptive support for their use in accordance with the present invention.

Moreover, the conclusion by the PTO is contrary to evidence submitted herewith by applicants. As demonstrated by Exhibits 1-3, one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because persons of skill in the art would have expected sufficiently related thermophilic organisms from the genus *Bacillus* (and now *Geobacillus*) to possess homologous *dnaX* nucleotide sequences or thermostable tau subunit proteins. Exhibits 1-3 confirm this expectation to have been reasonable.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 is improper and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other DNA molecules (encoding tau subunit proteins) within the scope of the claims. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Bacillus* (now *Geobacillus*) *stearothermophilus dnaX* (e.g., SEQ ID NO: 181) and describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42,

line 29), express the tau subunit encoded by such homologous *dnaX* sequences (see Example 21, expressing *A. aeolicus* tau subunit), and test the encoded tau subunit for clamp loader assembly competence (see Examples 24 and 25, testing *A. aeolicus* clamp loader assembly) and for clamp loader activity (see Examples 26 and 30, testing *A. aeolicus* clamp loader activity). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the *dnaX* homolog shown in Exhibit 1. For this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus* or *Bacillus* (now *Geobacillus*) *stearothermophilus dnaX* homologs.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 for lack of enablement is improper and should be withdrawn.

Because 1 is allowable for the reasons noted above, applicants further submit that new claims 10-16 also are allowable. Consistent with the PTO acknowledgments at pages 3-4 the outstanding office action, applicants further submit that that the specification provides written descriptive support for and enables the claimed DNA molecules that encode the tau subunit including the amino acid sequence of SEQ ID NO: 182 (i.e., claims 17-21).

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: August 24, 2006

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Exhibit 1



PubMed

Nucleotide

Protein

Genome

Structure

PMC

Taxonomy

OMIM

Books

Entrez Nucleotide

My NCBI

[\[Sign In\]](#) [\[Register\]](#)Search **Nucleotide**

for

Go**Clear**[Limits](#)[Preview/Index](#)[History](#)[Clipboard](#)[Details](#)Display **GenBank(Full)** Show **5** Send toRange: from **27312** to **28991****Show whole sequence**☐ Reverse complemented strand **Fe**☐ **1: BA000043. Reports** *Geobacillus kaust...*[gi:56378377][Links](#)[Features](#) [Sequence](#)

LOCUS BA000043 1680 bp DNA linear BCT 04-DEC-2004

DEFINITION *Geobacillus kaustophilus* HTA426 DNA, complete genome.

ACCESSION [BA000043](#) REGION: 27312..28991

VERSION [BA000043.1](#) GI:56378377

KEYWORDS .

SOURCE *Geobacillus kaustophilus* HTA426

ORGANISM *Geobacillus kaustophilus* HTA426

Bacteria; Firmicutes; Bacillales; Bacillaceae; *Geobacillus*.

REFERENCE 1

AUTHORS Takami,H., Takaki,Y., Chee,G.J., Nishi,S., Shimamura,S., Suzuki,H., Matsui,S. and Uchiyama,I.

TITLE Thermoadaptation trait revealed by the genome sequence of thermophilic *Geobacillus kaustophilus*

JOURNAL (er) *Nucleic Acids Res.* 32 (21), 6292-6303 (2004)

PUBMED [15576355](#)

REFERENCE 2 (bases 1 to 1680)

AUTHORS Takami,H., Takaki,Y. and Chee,G.

TITLE Direct Submission

JOURNAL Submitted (25-JUN-2003) Hideto Takami, Japan Marine Science and Technology Center, Microbial Genome Analysis Research Group; 2-15 Natsushima-cho, Yokosuka, Kanagawa 237-0061, Japan (E-mail:takamih@jamstec.go.jp, URL:<http://www.jamstec.go.jp/jamstec-e/bio/exbase.html>, Tel:81-46-867-9643, Fax:81-46-867-9645)

FEATURES

source Location/Qualifiers

1..1680

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/mol_type="genomic DNA"

/strain="HTA426"

/isolation_source="isolated from the deepest Ocean"

/db_xref="taxon:235909"

/note="thermophile"

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/gene="dnaX"

/locus_tag="GK0017"

CDS 1..1680

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/locus_tag="GK0017"

/EC_number="2.7.7.7"

/codon_start=1

/transl_table=11

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/protein_id="BAD74302.1"

/db_xref="GI:56378394"

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SLLDQAIISFSDGKLRLLDDVLAMTGAASFAALSSFIEATHRKDTAAVLQQLETMMQAQK
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ORIGIN

```
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481 aaaattccga cgacgatcat tcccgtgtc caacggttcg attttcgccg catcccgtt
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1201 gcgcccgtga aaaaactgtc caaaccgatg aaaacggggg gatataaagc cccggttggc
1261 cgcatttacg agctgttgaa acaggcgacg catgaagatt tagctttggt gaaaggatgc
1321 tgggcggatg tgctcgacac gttgaaacgg cagcataaag tgtcgcacgc tgccttgctg
1381 caagagagcg agccggttgc agcagcggcc tcagcgtttg tattaataat caaatacgaa
1441 atccactgca aaatggcgac cgatccaca agttcggtca aagaaaacgt cgaagcgatt
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1561 aaaataagag aagagttcat ccgcaataag gacgccatgg tggaaaaaag cgaagaagat
1621 ccgttaatcg ccgaagcgaa gcggctgttt ggcgaagagc tgatcgaaat taaagaataa
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Aug 15 2006 13:27:38

Exhibit 2

#####

Program: needle
Rundate: Wed Aug 23 15:47:53 2006
Align_format: srspair
Report_file: /ebi/extserv/old-work/needle-20060823-15475221809391.output
#####

#=====

Aligned_sequences: 2
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2: G_kaustophilus
Matrix: EBLOSUM62
Gap_penalty: 10.0
Extend_penalty: 0.5

Length: 1680
Identity: 1671/1680 (99.5%)
Similarity: 1671/1680 (99.5%)
Gaps: 3/1680 (0.2%)
Score: 10087.0

#=====

SEQ_181	1	GTGGCATACCAAGCGTTATATCGCGTGTTCGGCCGCAGCGCTTTGCGGA	50
G_kaustophilu	1	gtggcataccaagcggttatatcgcggtgttcggccgcagcgctttgcgga	50
SEQ_181	51	CATGGTCGGCCAAGAACACGTGACCAAGACGTTGCAAAGCGCCCTGCTTC	100
G_kaustophilu	51	catggtcggccaagaacacgtgaccaagacgttgcaaagcgccctgcttc	100
SEQ_181	101	AACATAAAATATCGCACGCTTACTTATTTTCCGGCCCGCGCGGTACAGGA	150
G_kaustophilu	101	aacataaaatatcgcacgcttacttattttccggcccgcgcggtacagga	150
SEQ_181	151	AAAACGAGCGCAGCGAAAAATTTTCGCCAAGGCGGTCAACTGTGAACAGGC	200
G_kaustophilu	151	aaaacgagcgcagcgaaaaattttcgccaaggcggtcaactgtgaacaggc	200
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G_kaustophilu	201	gccagcggcggagccatgcaatgagtgtccagcttgccctcggcattacga	250
SEQ_181	251	ATGGAACGGTTCCCGATGTGCTGGAAATTGACGCTGCTTCCAACAACCGC	300
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G_kaustophilu	351	ggccccgtacaaagtgtatatcatcgacgaggtgcatatgctgtcgatcg	400
SEQ_181	401	GTGCGTTTAAACGCGCTGTTGAAAACGTTGGAGGAGCCGCCGAAACACGTC	450
G_kaustophilu	401	gtgcgttttaaacgcgctgttgaaaacgttggaggagccgccgaaacacgtc	450
SEQ_181	451	ATTTTCATTTTGGCCACGACCGAGCCGCACAAAATTCGGCGCAGCATCAT	500
G_kaustophilu	451	attttcattttggccacgaccgagccgcacaaaattccgacgacgatcat	500

SEQ_181	501	TTCCCGCTGCCAACGGTTCGATTTTCGCCGCATCCCGCTTCAGGCGATCG	550
G_kaustophilu	501	ttcccgctgccaacggttcgattttcgccgcacccgcttcgggcgatcg	550
SEQ_181	551	TTTCACGGCTAAAGTACGTCGCAAGCGCCCCAAGGTGTCGAGGCGTCAGAT	600
G_kaustophilu	551	tttcacggctaaagtatgtcgcaagcgcccaagggtgtcgaggcggtccgat	600
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G_kaustophilu	601	gaggcattgtccgcccacgcccgtgctgcagacgggggatgcgcgatgc	650
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G_kaustophilu	701	tcgacgacgtgctggcgatgaccggggctgcatcatttgccgccttatcg	750
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G_kaustophilu	1151	cgggaattgcggcgcctgaaggaacaaccgcctgcccctccgctcgaccgcc	1200
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SEQ_181	1251	CCCGGTTGGCCGCATTTACGAGCTGTTGAAAACAGGCGACGCATGAAGATT	1300
G_kaustophilu	1251	cccggttggccgcatttacgagctgttgaaacaggcgacgcatgaagatt	1300

SEQ_181	1301	TAGCTTTGGTGAAAGGATGCTGGGCGGATGTGCTCGACACGTTGAAACGG	1350
G_kaustophilu	1301	tagctttggtgaaaggatgctgggcgatgtgctcgacacgttgaaacgg	1350
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SEQ_181	1651	GGCGAAGAGCTGATCGAAATTAAAGAA	1677
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Exhibit 3

CLUSTAL W (1.83) Multiple Sequence Alignments

Sequence format is Pearson

Sequence 1: SEQ_182 559 aa

Sequence 2: G_kaustophilus 559 aa

Start of Pairwise alignments

Aligning...

Sequences (1:2) Aligned. Score: 99

Guide tree file created: [/ebi/extserv/clustalw-work/interactive/clustalw-20060823-15474313.dnd]

Start of Multiple Alignment

There are 1 groups

Aligning...

Group 1: Sequences: 2 Score:11992

Alignment Score 3354

CLUSTAL-Alignment file created [/ebi/extserv/clustalw-work/interactive/clustalw-20060823-15474313.aln]

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:*****

SEQ_182      AVNCEQAPAAEPCNECPACLGITNGTVPDVLEIDAASNNRVDEIRDIREKVKFAPTSARY 120
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SEQ_182      KVYIIDEVHMLSIGAFNALLKTLEEPKHHVIFILATTEPHKIPATIIISRCQRFDFERRIPL 180
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*****:*****

SEQ_182      QAIVSRLKYVASAQGVEASDEALSAIARAADGGMRDALSLDDQAIISFSDGKLRLDDVLAM 240
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SEQ_182      TGAASFAALSSFIEAIHRKDTAAVLQHLETMMAQGKDPHRLVEDLILYYRDLLLYKTAPY 300
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SEQ_182      SAAAPSLASASELEPLIKRIETLEAELRRLKEQPPAPPSTAAPVKKLSKPMKTGGYKAPVG 420
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*****

SEQ_182      PLIAEAKRRLFGEELIEIKE 559
G_kaustophilus PLIAEAKRRLFGEELIEIKE 559
*****

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